Exhibit G

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

MITSUBISHI TANABE PHARMA CORPORATION, JANSSEN PHARMACEUTICALS, INC., JANSSEN PHARMACEUTICA NV, JANSSEN RESEARCH AND DEVELOPMENT, LLC, and CILAG GMBH INTERNATIONAL, Plaintiffs, v. MSN LABORATORIES PRIVATE LTD. and MSN PHARMACEUTICALS, INC., Defendants.	**Civil Action No. 17-5005 (consolidated)** **Contains Highly Confidential Information**

OPENING EXPERT REPORT OF ERIC J. MUNSON, PH.D.

I, Eric J. Munson, submit the following report on behalf of Mitsubishi Tanabe Pharma Corp., Janssen Pharmaceuticals, Inc., Janssen Pharmaceutica NV, Janssen Research and Development, LLC, and Cilag GmbH International (collectively, "Plaintiffs") in this action.

I. EXPERT QUALIFICATIONS

1. I am an expert in the field of pharmaceutical sciences, including the characterization of pharmaceuticals using various analytical techniques, with a specialty in the area of nuclear magnetic resonance ("NMR"), including both solution NMR and solid-state NMR spectroscopy ("SSNMR").

2. I graduated, *summa cum laude*, from Augustana College, Sioux Falls, South Dakota in 1987 with a Bachelor of Art degree in both Chemistry and Physics and a minor in Mathematics. I was also a Fulbright Fellow at the Technical University of Munich, Munich, West Germany from 1987-1988.

3. In 1993, I obtained a Ph.D. in Chemistry from Texas A&M University. My dissertation was in the field of solid-state NMR spectroscopy entitled "In Situ Solid-State Nuclear Magnetic Resonance Studies of Reactions in Zeolite Catalysts."

4. Currently, I am the Dane O. Kildsig Chair and Head of the Department of Industrial and Physical Pharmacy at Purdue University.

5. Prior to my current position at Purdue University, I was employed by the University of Kentucky, where I was the Patrick DeLuca Endowed Professor in Pharmaceutical Technology in the Department of Pharmaceutical Sciences from 2010-2018. Prior to 2010, I was employed at the University of Kansas for nine years, where I held the positions of Associate Professor, Courtesy Professor, and Professor in the Department of Pharmaceutical Chemistry. From 1994-2001, I was employed at the University of Minnesota in the Department of

Chemistry, where I held positions as an Assistant Professor, Associate Member of the Graduate Faculty, McKnight Land-Grant Assistant Professor, and Associate Professor. In addition, from 1993-1994, I was a Postdoctoral Associate at the University of California, Berkeley in the Department of Chemistry.

6. I am a member of various professional societies, including the American Chemical Society, the American Association of Pharmaceutical Scientists, and the American Association for the Advancement of Science.

7. I have also consulted with drug companies, both brand name and generic, on the characterization of pharmaceutical compounds and compositions. In addition, I have assisted both brand name and generic companies with litigation relating to pharmaceutical products.

8. In addition, I am a named co-inventor on three issued U.S. patents that all relate to NMR spectroscopy.

9. For a more complete list of my publications and patents, please see my curriculum vitae attached hereto as Exhibit 1.

10. I received a National Science Foundation Predoctoral Fellowship from 1988-1991. In 1991, I received the American Chemical Society Division of Analytical Chemistry Graduate Fellowship Award and the Society for Applied Spectroscopy Graduate Student Award. In 1993, I received the Texas A&M University Outstanding Graduate Research Award. I received the National Science Foundation CAREER Award in 1996. In 2003, I received the Pfizer Research Scholar Award. In 2009, I was a Fellow at American Association of Pharmaceutical Scientists. In 2014, I received the Research Achievement Award from the Analysis and Pharmaceutical Quality Section of the American Association of Pharmaceutical Scientists (AAPS).

11. From 2012-2015, I was an associate editor for the journal *Molecular Pharmaceutics*.

12. For a more complete list of my honor and awards, please see my curriculum vitae attached hereto as Exhibit 1.

13. I have given over 200 invited lectures on the topics of SSNMR, including, but not limited to, SSNMR of pharmaceuticals, SSNMR studies of polymorphism, new techniques for SSNMR studies, and SSNMR spectroscopy to characterize polymorphs.

14. For a more complete list of my invited lectures, please see my curriculum vitae attached hereto as Exhibit 1.

15. I have also published in the areas of X-Ray Powder Diffraction ("XRPD") analysis, including publications that include both SSNMR and XRPD data as techniques to characterize polymorphic forms of compounds:

- Padden, B. E.; Zell, M. T.; Dong, Z.; Schroeder, S. A.; Grant, D. J. W.; Munson, E. J. "Comparison of Solid-State NMR Spectroscopy and Powder X-Ray Diffraction for Analyzing Mixtures of Polymorphs: 1. Neotame", *Anal. Chem.* 1999, *71*, 3325-3331;
- Liang, Jingmei; Ma, Yue; Chen, Bin; Munson, Eric J.; Davis, H. Ted; Binder, David; Chang, Hung-Ta; Abbas, Syed; Hsu, F.-L. "Solvent modulated polymorphism of sodium stearate crystals studied by X-ray diffraction, solid-state NMR, and cryo-SEM", *J. Phys. Chem. B* 2001, *105*, 9653-9662;
- Delaney, S.P.; Nethercott, M.J.; Mays, C.J.; Winquist, N.T.; Arthur, D.; Calahan, J.L.; Sethi, M.; Pardue, D.S.; Kim, J.; Amidon, G.; Munson, E.J. "Characterization of Synthesized and Commercial Forms of Magnesium Stearate Using Differential Scanning Calorimetry, Thermogravimetric Analysis, Powder X-Ray Diffraction, and Solid-State NMR Spectroscopy", *J. Pharm. Sci.*, 2017, *106*, 338-347.

16. I am being compensated at my usual rate of $350 per hour in connection with this proceeding. My compensation does not depend in any way on the outcome of this litigation.

II. PREVIOUS TESTIMONIAL EXPERIENCE

17. In the last four (or more) years, I have provided expert testimony at trial or by deposition in the following cases:

- *Bristol-Myers Squibb Company and Pfizer Inc. v. Aurobindo Pharma USA Inc.* (Case No. 17-374-LPS-consolidated, D. Del.)
- *Novartis Pharmaceuticals Canada Inc. v. Teva Canada Limited and The Minister of Health* (Court File No. T-1260-16);
- *Merck Sharp & Dohme Corp. v. Fresenius Kabi USA, LLC., et al.* (Case No. 14-4989 (SRC)(CLW)); and
- *Merck Sharp & Dohme Corp. v. Xellia Pharms. Aps., et al.* (Case No. 14-199-RGA (D. Del.)).

III. BASES FOR OPINIONS

18. The opinions presented below are based upon my education, experience, and consideration of the information and materials referred to herein, as well as those listed in Exhibit 2. Exhibit 2 includes a table identifying the exhibits cited in this report.

IV. OVERVIEW OF OPINIONS

19. I understand that the Defendants MSN Laboratories Private Ltd. and MSN Pharmaceuticals, Inc. (collectively, "MSN") seek permission from the FDA to market generic versions of Invokana® through its submission of Abbreviated New Drug Application No. 210462 ("the '462 ANDA").

[redacted]

[redacted]

23. I am also prepared to serve in a teaching capacity to discuss scientific principles relating to my areas of expertise, as well as the level of ordinary skill in the art at the relevant time(s) and background relating to the issues discussed herein, if asked to do so.

V. A PERSON OF ORDINARY SKILL IN THE ART

24. I was asked by counsel to use December 4, 2006, the filing date of the provisional application to which the '582 patent claims priority, as the relevant date for my analysis. While my report is based on that date, my opinions would not change if I used December 3, 2007, the non-provisional filing date of the '582 patent, as the relevant date for my analysis.

25. In my opinion, as of either December 4, 2006 or December 3, 2007, a person of ordinary skill in the art ("POSA") would be (a) a person with an advanced degree in chemistry, analytical chemistry, physical chemistry, organic chemistry, pharmaceutical chemistry, medicinal chemistry, or chemical engineering, and with at least two years of experience developing, characterizing, and/or analyzing pharmaceutical compounds and products; or (b) a person with a bachelor's degree in one of those disciplines and several years of practical experience in researching, developing, characterizing, and/or analyzing crystals and/or

polymorphs in solid-state chemistry. I am a person of at least ordinary skill under this definition. The opinions I express in the report are from the viewpoint of a POSA as I have defined it.

VI. LEGAL STANDARDS REGARDING PATENT INFRINGEMENT

26. In forming my opinions in this case, I used the following legal standards that were provided to me by counsel.

27. I understand that the plaintiff bears the burden of proving patent infringement by a preponderance of the evidence. It is my understanding that the plaintiff must show that the defendant's accused product meets each and every claim limitation properly construed.

28. I understand that it is an act of infringement to submit an ANDA for a drug product claimed in a patent or the use of which is claimed in a patent. It is my further understanding that it is an act of infringement to make, use, sell, offer to sell, or import into the United States a product claimed by a patent. It is my further understanding that in the context of an ANDA, the question for infringement is whether, if the drug product in question were approved based on the ANDA, would the manufacture, use, sale, or offer to sell that drug product infringe the patent. Put differently, the question is whether the products that are made, used, sold, or offered for sale pursuant to that ANDA will likely include products that infringe.

29. I understand that infringement involves a two-step analysis. The first step is determining the proper construction of the asserted claims. I have reviewed the claim constructions that have been adopted in this case, as I discuss below.

30. I understand that the second step in the infringement analysis is to compare the properly construed claims to the accused products. The accused products infringe if they meet every element of a properly construed claim.

31. I understand that the Court has issued a claim construction order in this case. I understand that the Court has ruled that the term "crystalline form of 1-(β-D-glucopyranosyl)-4-methyl -3-[5-(4-fluorophenyl)-2-thienylmethyl]benzene hemihydrate," as it appears in claims 1 and 3 of the '582 patent means "a crystalline form of 1- (β-D-glucopyranosyl)-4-methyl-3-[5-(4-fluorophenyl)-2-thienylmethyl]benzene comprising approximately half a mole of water to one mole of the compound". (Ex. 4, *Markman* Order at Dkt. No. 237.)

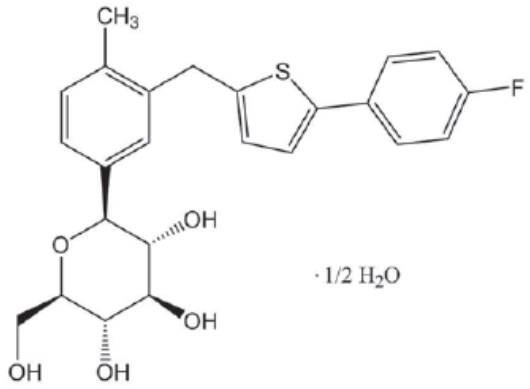
32. I have considered and applied the Court's Claim Construction in my analysis of the '582 patent. To the extent any terms of the claims have not been construed by the parties or the Court, I understand that those claim terms should be interpreted as they would have been understood by a POSA at the time of the respective patent applications.

VII. BACKGROUND

A. The '582 patent

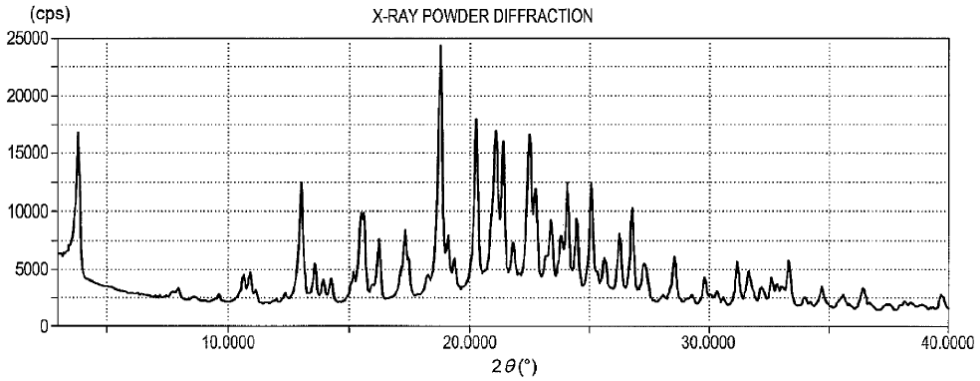
33. The '582 patent is entitled "Crystalline form of 1-(β-D-glucopyranosyl)-4-methyl-3-[5-(4-fluorophenyl)-2-thienylmethyl]benzene hemihydrate." 1-(β-D-glucopyranosyl)-4-methyl-3-[5-(4-fluorophenyl)-2-thienylmethyl]benzene is a chemical name for canagliflozin.

34. Canagliflozin hemihydrate has the following chemical structure:



(Ex. 22.)

35. Figure 1 of the ’582 patent is an XRPD[1] pattern of an embodiment of crystalline canagliflozin hemihydrate:



(Ex. 3, ’582 patent at Fig. 1).

36. Claim 1 of the ’582 patent recites: “A crystalline form of 1-(β-D-glucopyranosyl)-4-methyl-3-[5-(4-fluorophenyl)-2-thienylmethyl]benzene hemihydrate.”

37. Claim 3 of the ’582 patent recites: “A crystalline form of 1-(β-D-glucopyranosyl)-4-methyl-3-[5-(4-fluorophenyl)-2-thienylmethyl]benzene hemihydrate of claim 1, having substantially the same X-ray diffraction pattern as set out in FIG. 1.”

B. MSN’s Proposed ANDA Products

38. I understand that MSN has submitted the ’462 ANDA to the United States Food and Drug Administration (“FDA”) and seeks to market generic canagliflozin tablets in 100 mg and 300 mg tablets (“MSN’s ANDA Products” or the “ANDA Products”) under the ’462 ANDA. I understand that upon receiving approval from the FDA of its ANDAs, MSN intends to market its proposed ANDA Products in the United States.

[1] XRPD can also be referred to as PXRD, powder X-ray diffraction, or powder-XRD.

[redacted]

C. Methods to Characterize Solid Forms of Compounds

42. When a compound has been the subject of sufficient research and development regarding its solid-state structural properties, it may be possible to develop experimental protocols to identify whether a sample contains a given solid-state form. Those experimental protocols can consist of one or more analytical methods. In the sections below, I discuss two of those methods in more detail: XRPD and SSNMR, and more specifically fluorine-19 ("^{19}F") SSNMR.

1. X-Ray Powder Diffraction

43. XRPD is an analytical technique that can be used to identify the form of a crystalline compound, such as crystalline canagliflozin hemihydrate, and distinguish between different crystalline forms, which are colloquially referred to as "polymorphs." XRPD has been used to distinguish solid-state forms for decades, and is a standard technique in the field. (Ex. 7 at 2445-46.)

44. Where sufficient research and development has occurred on the solid-state properties of a compound using various analytical techniques, the unique XRPD pattern can be identified for different forms of the compound. Thus, it can be possible to develop an XRPD method that can be used to identify solid-state forms (polymorphs) of a compound in a given sample.

45. In XRPD (as used herein), X-rays are directed at a powder sample and the X-rays diffracted by the sample are detected by a diffractometer. A sample is placed within the XRPD instrument and the structures within the sample diffract incident radiation, or X-rays, based on the orientation of the molecules. For crystalline materials, different crystalline structures typically diffract X-rays at different "scattering angles" (the angle of the incident X-ray beam to the crystal where scattering of the X-rays is observed) and at different "intensities" (how many X-rays are scattered). The scattering angles are measured and reported as diffraction peaks as a function of two theta ("2θ") ± 0.2 degrees 2θ. The 2θ values can be plotted against the differing intensities as "lines" or "peaks" to produce a diffraction pattern.

2. Solid-State NMR Spectroscopy (SSNMR)

a. General Background

46. SSNMR is an analytical technique that can be used to identify the form of a crystalline compound, such as crystalline canagliflozin hemihydrate, and distinguish between different polymorphs. SSNMR has been used to distinguish crystalline forms of a compound in the pharmaceutical field since at least the 1980's and is a standard technique in the field. (Ex. 8 at 2591-2605.)

47. SSNMR can be used in conjunction with other analytical techniques to determine what solid-state forms of a compound are contained within a given sample. For example, the SSNMR spectrum of solid-state forms can be obtained to determine the SSNMR characteristic peaks for different forms of a compound. Thus, it can be possible to develop a SSNMR method that can be used to identify solid-state forms (polymorphs) of a compound in a given sample.

48. In SSNMR, several techniques are used to obtain a high-resolution SSNMR spectrum of a sample. These techniques include magic-angle spinning, cross polarization, and high-power decoupling, described in more detail below.

49. SSNMR involves placing a sample into a very strong and homogeneous magnetic field. After being placed in the magnetic field, certain nuclei can be thought of as acting as small magnets that are precessing[2] about an axis within the magnetic field. The NMR active nuclei in the sample align themselves approximately equally with and against the magnetic field, with a slight excess being aligned with the magnetic field. As the sample is pulsed with radio waves, some of the precessing nuclei will absorb this energy and flip their spin to oppose the magnetic field. These flipped nuclei are now precessing in a higher energy state. After the pulse, the

[2] "Precession" is the rotation of the axis of a spinning body. A common example is the wobbling of a spinning top.

nuclei begin to flip back to their original spin state, a process called relaxation that can take up to several seconds or even minutes for particular nuclei (*i.e.*, T_1 relaxation time). The precessing rate of the nuclei is detected and recorded by the SSNMR spectrometer. These precessing rates are then transformed into spectra, which contain information about the composition of the sample and chemical structure.

50. The NMR activity of a nucleus in the magnetic field is partially determined by the atom's atomic number (*i.e.*, number of protons in the nucleus of the atom) and mass number (*i.e.*, number of protons and neutrons in the nucleus of the atom). If both numbers are even, then the nucleus is not observable by SSNMR. If either is odd, then it is possible to observe the nucleus with SSNMR. This concept is important because an element, which always has the same number of protons in the nucleus, can have multiple isotopes, each with a different number of neutrons in the nucleus. Only certain isotopes produce an NMR signal, and therefore are useful for SSNMR, and it is often preferred to study non-quadrupolar nuclei. Compositions that contain one or more of the following nuclei are commonly analyzed using SSNMR spectroscopy: ^{13}C ("carbon-13"), ^{1}H ("proton"), ^{15}N ("nitrogen-15"), and ^{19}F ("fluorine-19"). All of these nuclei are non-quadrupolar. The sample being analyzed dictates the choice of nuclei to monitor by SSNMR. The natural abundance of the isotope also needs to be considered when deciding which isotope to monitor by SSNMR.

51. The following figure, from an article I co-authored, shows an example of SSNMR spectra of a non-quadrupolar nucleus (in this case ^{13}C) where magic-angle spinning, cross polarization, and high-power proton decoupling were applied and resulted in a high-resolution SSNMR spectrum of a pharmaceutically-related compound:

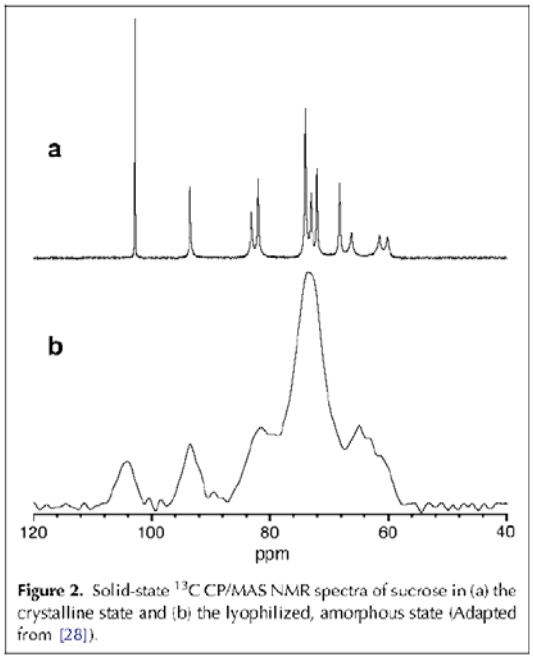


Figure 2. Solid-state ^{13}C CP/MAS NMR spectra of sucrose in (a) the crystalline state and (b) the lyophilized, amorphous state (Adapted from [28]).

(Ex. 9 at 981.)

52. A SSNMR spectrum is composed of peaks, with an x-axis that corresponds to chemical shifts, which are in units of parts per million (ppm), and a y-axis corresponding to peak intensity. Peaks in a SSNMR spectrum are located at chemical shifts that are a function of the local electronic environment surrounding the nucleus of an atom. In SSNMR, the electronic environment is affected by the functional groups of the compound, and by how the molecules are packed together (i.e., crystalline forms, or amorphous). (Ex. 8 at 2593.) Thus, the chemical shifts of the peaks in a SSNMR spectrum can give information about both the functional groups in a compound and a compound's solid-state form. (*Id.*)

53. SSNMR can determine whether a solid sample contains crystalline material or material that is amorphous. Crystalline forms have peaks where the "line widths" of the peaks (i.e. the full width at half height of the peaks) are typically about an order of magnitude less than the corresponding amorphous form of the material. In other words, a material in crystalline form has sharper/narrower SSNMR peaks than the corresponding amorphous form. A typical

amorphous line width in ^{13}C SSNMR is 3-5 ppm, whereas crystalline peaks have line widths that are typically at about 1 ppm or less. In the figure I referenced above, the spectra is for sucrose in the crystalline state (a) and sucrose in the amorphous state (b):

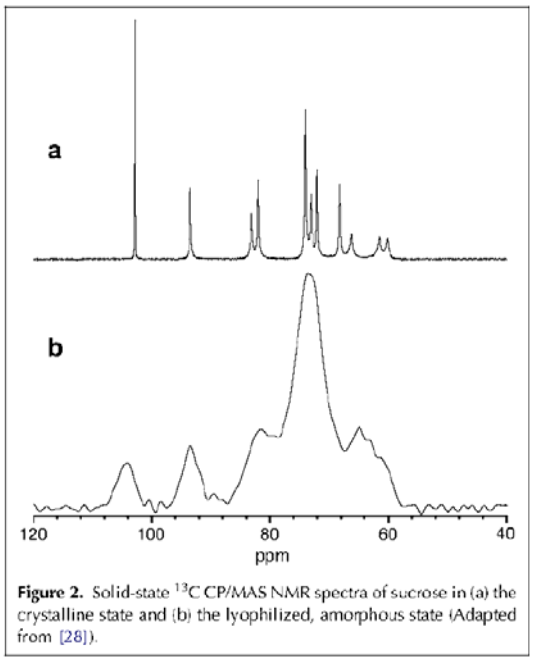


Figure 2. Solid-state ^{13}C CP/MAS NMR spectra of sucrose in (a) the crystalline state and (b) the lyophilized, amorphous state (Adapted from [28]).

(Ex. 9 at 981.) As can be seen in this example, the peaks for the crystalline material are sharper and narrower than the amorphous material. A similar type of change occurs for the other nuclei discussed previously, and in particular in ^{19}F SSNMR.

b. Flourine-19 SSNMR

54. ^{19}F SSNMR spectroscopy is a particularly powerful technique for investigating pharmaceutical compounds compared with studying other NMR active nuclei. When ^{19}F is present in a pharmaceutical compound, ^{19}F SSNMR can provide detailed information about crystalline forms as compared to amorphous forms, as well as different crystalline forms that may be present in a formulation. One advantage of ^{19}F SSNMR is that pharmaceutical excipients do not typically contain ^{19}F, and thus do not generate peaks in a ^{19}F SSNMR spectrum. In other words, if a peak is observed in a ^{19}F SSNMR spectrum, one knows that the peak was not created

by one of the excipients. For MSN's ANDA Products, I know that any peaks in the ^{19}F SSNMR spectrum are from canagliflozin because none of the excipients used by MSN in its ANDA Products contain fluorine.

55. Another advantage of ^{19}F SSNMR, compared with SSNMR of other commonly-observed nuclei, is that ^{19}F is an NMR-active nuclei that is approximately 100% naturally abundant. That means that essentially all fluorine atoms will generate a SSNMR signal. By contrast, carbon atoms contain only (1.1%) of ^{13}C nuclei, with most of the rest of the carbon atoms containing the NMR inactive ^{12}C nuclei. Nitrogen atoms contain only 0.34% of ^{15}N nuclei, with most of the rest of the nitrogen atoms containing ^{14}N, which is a quadrupolar nucleus.

c. Techniques for Obtaining a High-Resolution ^{19}F SSNMR Spectrum

56. In order to acquire a high-resolution ^{19}F SSNMR spectrum in the solid state, there are several techniques that should generally be applied, and which were applied in my work on this project. (*See, e.g.*, Ex. 8; Ex. 9; Ex. 10.) The first is called magic-angle spinning ("MAS"). MAS is a technique that takes broad SSNMR signals and makes them sharper in a SSNMR spectrum. Solid samples have molecules, or groups of molecules, that are fixed in their orientation in the magnetic field. These fixed orientations result in a distribution of chemical shifts for the sample, known as chemical shift anisotropy, which broadens the peaks in the spectrum. MAS is performed by spinning the sample at an angle of 54.7 degrees with respect to the static magnetic field. When this occurs, the distribution of chemical environments is averaged so that only the isotropic, or average, chemical-shift value is observed. This makes the peaks narrower, thereby improving resolution and making it easier to distinguish different peaks from each other. However, one potential result of MAS is the generation of artifacts in the SSNMR spectra called "spinning sidebands." Spinning sidebands appear at known locations in

the SSNMR spectrum that are defined by how fast the sample was spun. If necessary, spinning sidebands can be separated from the isotropic chemical shifts by varying the spinning speed of the sample. When the spinning speed of the sample is changed, the chemical shifts of the isotropic speed will not change, but the spinning sidebands will change at known values based upon the spinning speed.

57. A second technique that is used to improve the resolution of a ^{19}F SSNMR spectrum is to decouple the protons (i.e. ^{1}H nuclei) from the ^{19}F nuclei. In the solid state, the fixed orientations of the protons that are coupled to ^{19}F may result in a broadening of the peaks in the ^{19}F SSNMR spectrum. By applying a strong radiofrequency signal at the resonance frequency of the protons, the protons can be "decoupled" from ^{19}F, resulting in a narrower peak in the ^{19}F SSNMR spectrum.

58. Another technique that can improve the efficiency of ^{19}F SSNMR is called "cross polarization." In ^{19}F SSNMR, the spin-lattice relaxation times (T_1) of the ^{19}F SSNMR nuclei may be very long. Longer relaxation times mean that a fewer number of individual data acquisitions can be added together in a given amount of time. Fewer acquisitions means a worse signal to noise ratio, leading to relatively poorer sensitivity compared to the sensitivity that would otherwise be obtained with more acquisitions. Cross polarization is a method that uses the relaxation time of a different nucleus, such as a hydrogen nucleus (a proton or ^{1}H), which has a shorter relaxation time, to increase the number of acquisitions per unit time, resulting in increased sensitivity. In addition, cross polarization can be used to improve the signal to noise ratio of the spectrum for certain nuclei. Cross polarization typically works by transferring magnetization from abundant nuclei, such as ^{1}H, to less abundant nuclei, such as ^{13}C, that often have a long T_1 relaxation time as well as a low magnetogyric ratio, which for ^{13}C is one-quarter

of the value compared to ^{1}H. The proton or ^{1}H nuclei transfer their magnetization to nearby ^{13}C nuclei, which then relax and the signal is collected. In ^{19}F SSNMR, cross-polarization can sometimes be beneficial because the proton relaxation time is often much shorter than the fluorine relaxation time.

59. When SSNMR is conducted properly, the technique gives consistent results for a well-characterized compound. Different samples of a compound typically will generate the same peaks at about the same location in a ^{19}F SSNMR spectrum ± 0.4 ppm.[3]

d. Techniques for Selectively Observing Forms in a SSNMR Spectrum

60. When there are two or more components in a sample, it is possible with SSNMR to selectively reduce the signal from certain components based upon the SSNMR properties of those components. Components in this case can refer to different compounds, or even the same compound but in different forms, e.g. crystalline and amorphous, or two different crystalline forms. This approach is especially useful when the component of interest is present at lower levels in the sample. For example, when a sample contains a crystalline form mixed with a larger amount of the amorphous form of the same compound, the strong signal from the amorphous material can make it difficult to detect the signal from the crystalline material.

61. One method to selectively observe a component present at relatively lower levels in a sample with a mixture of components is to use an approach described here as the "$T_{1\rho}$ spin lock." This method utilizes differences in the spin-lattice relaxation time in the rotating frame (referred to as $T_{1\rho}$) between different components of the mixture. For example, amorphous and

[3] ^{19}F SSNMR has a margin of error of typically ±0.4 ppm, depending upon linewidth. Because the location of peaks can be affected by the reference point, which can shift slightly, the location of the peaks for a particular compound can vary slightly when tested on different machines or if the spectra were referenced slightly differently. Differences in referencing will result in a consistent shift of all of the peak locations in the spectrum.

crystalline materials can have very different proton $T_{1\rho}$ values. (Ex. 8; Ex. 10.) In particular, the nuclei of crystalline materials can have significantly longer $T_{1\rho}$ relaxation times than the nuclei of amorphous materials, and in particular, longer proton $T_{1\rho}$ relaxation times. That is because the higher molecular mobility in the amorphous form provides a mechanism for relaxation. (Ex. 8.)

62. When a particular crystalline component has a significantly longer proton $T_{1\rho}$ relaxation time compared to the amorphous component, we can select the settings of the ^{19}F SSNMR experiment to detect the signal from the crystalline material that is mixed with the amorphous material. When we increase the proton spin-locking time, the signals generated by nuclei that have a short proton $T_{1\rho}$ relaxation time will decay more quickly, while the signals generated by nuclei that have a long proton $T_{1\rho}$ relaxation time will decay more slowly. As a result of this phenomenon, at longer proton spin-locking times, signals from amorphous materials with a short relaxation time will have decayed more significantly than signals from crystalline materials with a long relaxation time. Thus, one can more readily detect signals from crystalline materials in a mixture of amorphous and crystalline materials by setting higher proton spin locking times.

63. Consider an example where the amorphous material's relaxation time ($T_{1\rho}$) is 10 ms and the crystalline relaxation time ($T_{1\rho}$) is 80 ms. If we set the proton spin-locking time at 50 ms, 99.3% of the amorphous signal would no longer be present due to natural decay. By contrast, only 54% of the crystalline signal would no longer be present due to natural decay. As a result, the low signal from the amorphous material at the 50 ms collection time does not obscure the signal from the crystalline material. This method can therefore be used to focus on detection of the signal from the crystalline material.

64. My colleagues and I have published several papers containing examples that show how differences between the proton $T_{1\rho}$ values of crystalline and amorphous forms of compounds can be used to detect and identify the crystalline component in a sample that contains primarily amorphous material. (Ex. 8; Ex. 10.)

65. In the Sotthivirat article, I used this approach to detect the presence of crystalline prednisolone (PDL) in a mixture with amorphous cyclodextrin (CD). (Ex. 10.) I have reproduced Figure 3 of the Sottivirat paper for reference below. Figure 3 shows graphically how the signal intensity decreases significantly for the material with the short $T_{1\rho}$ relaxation time, cyclodextrin or CD, whereas the signal intensity of the material with the long $T_{1\rho}$ relaxation time, prednisolone or PDL, does not decrease significantly. This example illustrates that this technique can be used to detect the signal from the crystalline material in the presence of a larger amount of amorphous material in the sample. Even though the example is shown for ^{13}C SSNMR, the method is equally applicable to both ^{13}C and ^{19}F SSNMR.

66. Below, I have reproduced Figures 3b-3d from the Sottivirat paper, which show how the technique works. Figure 3b is the spectrum of the crystalline prednisolone acquired using a 2 ms contact time and Figure 3c is the mixture of the amorphous cyclodextrin and crystalline prednisolone acquired using a 2 ms contact time. In Figure 3c, even though the prednisolone is less than 10% of the formulation by weight, the peaks are very evident in the spectrum. In Figure 3d, $T_{1\rho}$ spin lock is applied to the same sample used in Figure 3c and the crystalline prednisolone peaks are even more evident in the spectrum.

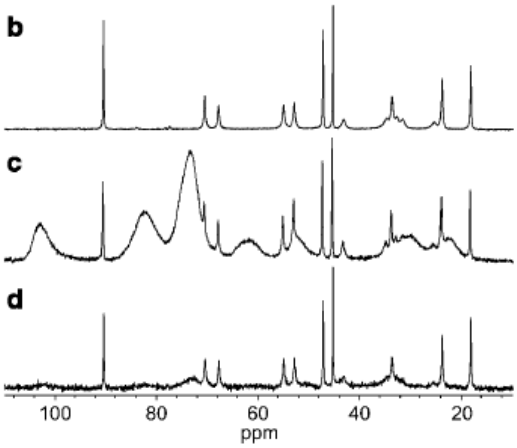


Figure 3. (a) Plot of normalized CD and PDL peak areas as a function of contact time, and ^{13}C solid-state NMR spectra from 10–110 ppm of (b) crystalline PDL form II acquired with a 2-ms contact time; (c) a physical mixture of CD and PDL form II in a 2:1 CD to PDL molar ratio, acquired using a 2-ms contact time; and (d) a physical mixture of CD and PDL form II in a 2:1 CD to PDL molar ratio, acquired using a 7-ms contact time.

(Ex. 10 at 1011.)

D. Characterization of Solid Forms of Canagliflozin

67. Canagliflozin is a compound that has been extensively studied for over ten years and has been well characterized by multiple testing techniques, including XRPD, NMR, SSNMR, Raman spectroscopy, IR spectroscopy, DSC, and TGA. In addition, the full 3-D crystal structure of crystalline canagliflozin hemihydrate has been determined. (*See* Ex. 11 at 734-736.) [redacted]

69. As noted above, the canagliflozin hemihydrate crystal structure above has two molecules of canagliflozin and one molecule of water. Canagliflozin hemihydrate has approximately half a molecule of water for every molecule of canagliflozin.

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4 [redacted]

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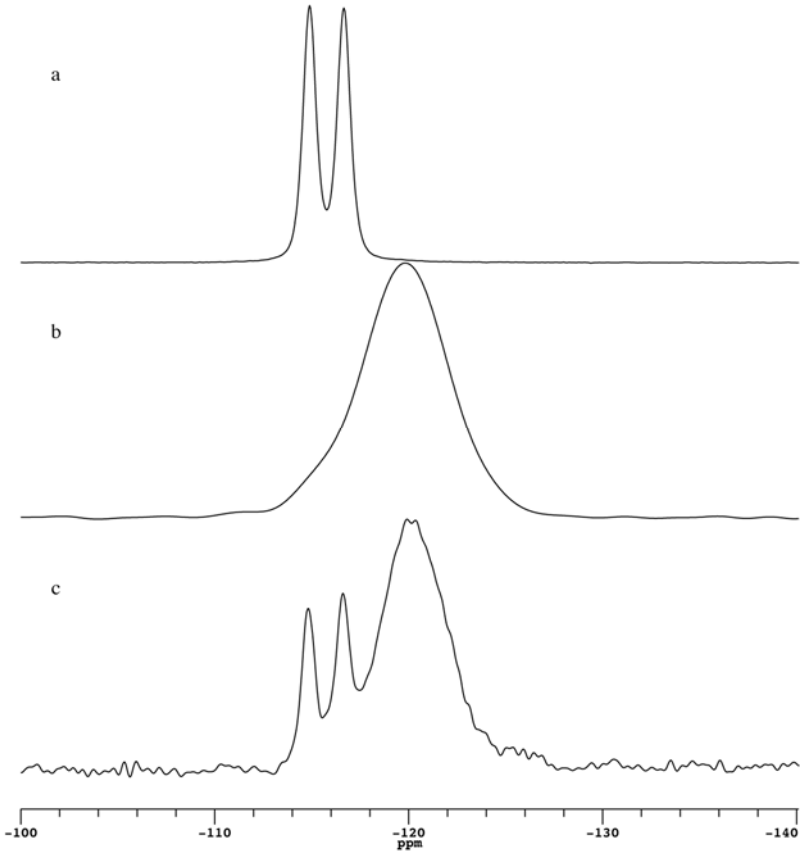
For example, levofloxacin, which also has two molecules in the asymmetric unit for the fluorine atom attached to the phenyl ring,

had ^{19}F SSNMR chemical shifts of -114.8 and -116.6 ppm with line widths of 370 and 380 Hz, respectively, shown as (a) in the figure below. (Ex. 12.) By contrast, amorphous levofloxacin had a single peak located at -119.7 ppm with a line width of ~2300 Hz, shown as (b) in the figure below. (*Id.*)



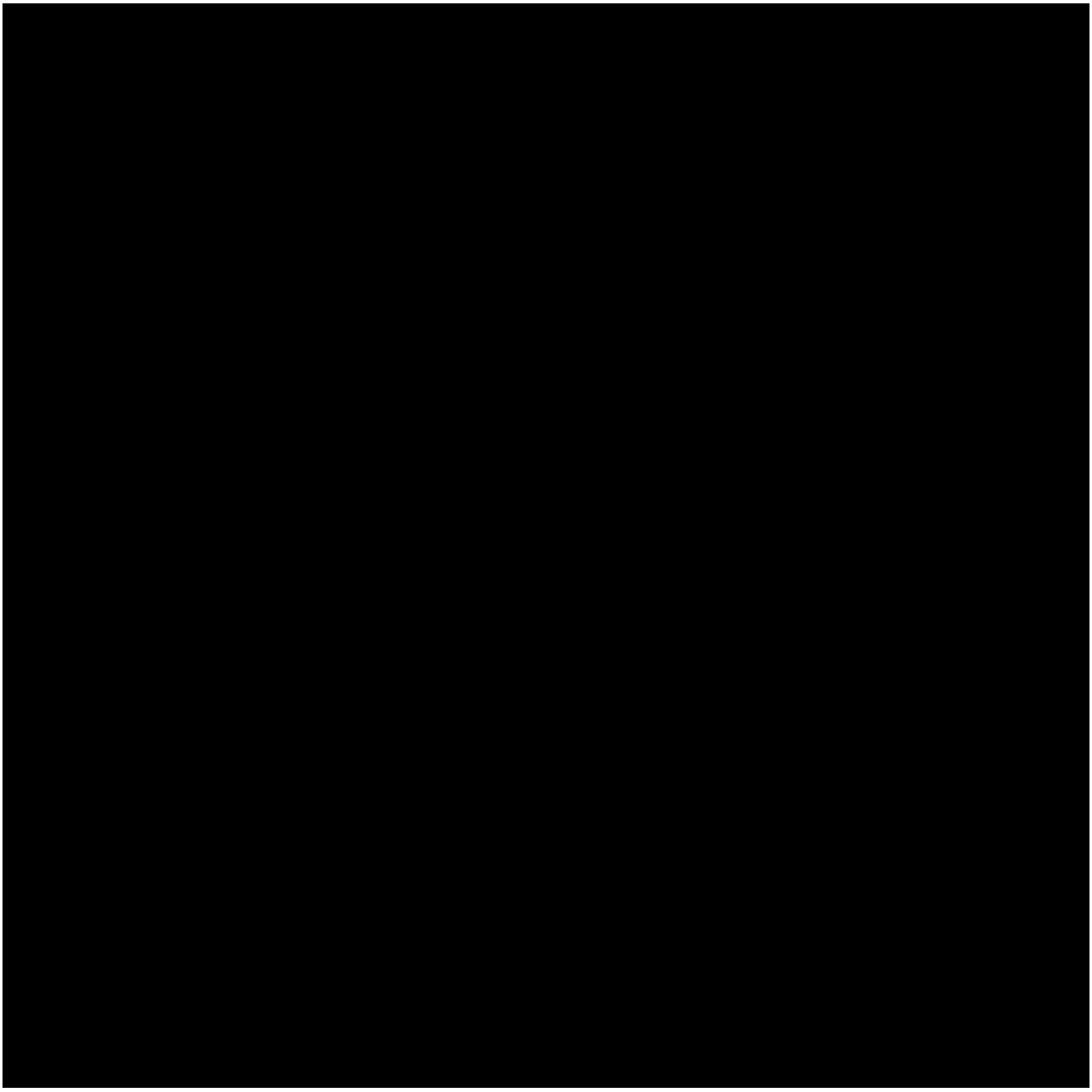
^{19}F SSNMR spectra of a) as-received levofloxacin, b) spray-dried levofloxacin, and c) sample b) collected 10 minutes after the initial acquisition.

[redacted]

VIII. MATERIALS AND METHODS

76. Below are the details for the samples analyzed, the chain of custody, and the analytical methods applied.

[redacted]



[redacted]

[5] I have a partial ownership interest in and am a Senior Consultant at Kansas Analytical Services, and routinely direct work conducted there.

[redacted]

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IX. ANALYSIS & DISCUSSION

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X. SUPPLEMENTATION

163. I reserve the right to supplement or amend my report in response to opinions expressed by MSN's experts, or in light of additional evidence, testimony, discovery, or other information that may be provided to me after the date of this report.

164. I also reserve the right to offer additional testimony, if necessary, concerning the subject matter of the patents-in-suit.

165. In addition, I expect that I may be asked to consider and testify about issues that may be raised by MSN's fact witnesses and technical experts at trial or in their reports. It may also be necessary for me to supplement my report as a result of ongoing discovery, Court rulings and testimony at trial.

XI. TRIAL EXHIBITS

166. I may rely on visual aids and demonstrative exhibits that demonstrate the bases for my opinions. These visual aids and demonstrative exhibits may include, for example, interrogatory responses, deposition testimony and exhibits, as well as charts, photographs, diagrams, videos, and animated or computer-generated videos.

Executed this 7th day of February 2020. I declare under penalty of perjury that the foregoing is true and correct.

Eric J. Munson, Ph.D.